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L2 and glucomannan	8

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Set Name Query

side by side

DB=USPT; PLUR=YES; OP=ADJ

L4 L2 and glucomannan

L3 L2 and (immunoferon or immunoferon or glycoposphopeptical)

L2 L1 and asthma\$3

L1 ((514/25 |514/42 |514/54 |514/62)!.CCLS. |(536/18.7 |536/123.1 |536/123.12 |536/124)!.CCLS.)

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result set

8 L40 L3144 L24488 L1

END OF SEARCH HISTORY

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN **87139-86-4** REGISTRY

CN Immunoferon (9CI) (CA INDEX NAME)

OTHER NAMES:

CN AM 3

CN Glicofosfopeptical

MF Unspecified

CI MAN

LC STN Files: BIOSIS, CA, CANCERLIT, CAPLUS, CIN, DDFU, DRUGU, IPA,
MEDLINE, PHARMASEARCH, PROMT, TOXCENTER, USPATFULL, VETU

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

16 REFERENCES IN FILE CA (1962 TO DATE)

16 REFERENCES IN FILE CAPLUS (1962 TO DATE)

(FILE 'HOME' ENTERED AT 16:32:34 ON 03 MAR 2003)

FILE 'REGISTRY' ENTERED AT 16:32:43 ON 03 MAR 2003

L1 1 S IMMUNOFERON/CN
L2 0 S GLYCOPHOSPHOPEPTICAL/CN

FILE 'CAPLUS, MEDLINE, USPATFULL' ENTERED AT 16:33:59 ON 03 MAR 2003

L3 2 S L1
L4 24 S IMMUNOFERON/CN

FILE 'REGISTRY' ENTERED AT 16:35:26 ON 03 MAR 2003

L5 1 S IMMUNOFERON/CN

FILE 'USPATFULL, CAPLUS, MEDLINE' ENTERED AT 16:36:12 ON 03 MAR 2003

L6 43 S L1 OR L5
L7 3 S L6 AND (ASTHMA OR ALLEG?)
L8 0 S GLICOFOSFOPEPTICAL/CN

FILE 'REGISTRY' ENTERED AT 16:41:06 ON 03 MAR 2003

L9 1 S GLICOFOSFOPEPTICAL/CN
L10 1 S IMMUNOFERON/CN
L11 1 S IMMUNOFERON/CN
L12 0 S GLYCOPHOSPEPTICAL/CN

FILE 'CAPLUS, MEDLINE, USPATFULL' ENTERED AT 16:43:13 ON 03 MAR 2003

L13 43 S L9 OR L10 OR L11
L14 328 S NIGELLA SATIVA
L15 3 S L13 AND (ASTHMA OR ALLERGY)

L7 ANSWER 1 OF 3 USPATFULL

ACCESSION NUMBER: 2002:119853 USPATFULL
TITLE: **Asthma**/allergy therapy that targets
T-lymphocytes and/or eosinophils
INVENTOR(S): Nassief, Nida Abdul-Ghani, Doha, IRAQ

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002061841	A1	20020523
APPLICATION INFO.:	US 2001-944564	A1	20010904 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-4777	19990302
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	AL-JASSIM, Rawaa, 2578 River Woods Drive, Naperville, IL, 60565	
NUMBER OF CLAIMS:	24	
EXEMPLARY CLAIM:	1	
LINE COUNT:	772	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition for the treatment and/or prophylaxis of diseases caused by type I hypersensitivity reactions consisting essentially of Glicophosphopeptical, or pure Nigella Sativa seeds, in a concentration which stimulate Th1 lymphocytes and selectively switch-off the eosinophilic airway inflammation

A method of treatment of allergy using Th1 stimulating agents, to be administered to a mammal such as human in need of such treatment in a shot of 5 days only, resulted in significant decrease in symptom score started day 3, and in sputum eosinophils by day 14, followed by long-term clinical remission of a mean of 6 months.

The BCG-like Th1 stimulation is also used in treating diseases in which the body defensive mechanism is a Cell Mediated Immunity, including viral infections, as but not limited to influenza and common cold, Chronic and recurrent urinary tract infection, pelvic inflammatory diseases as neuroimmune appendicitis, cancer, crohns disease and facial palsy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:627968 CAPLUS
DOCUMENT NUMBER: 133:202992
TITLE: Glycophosphopeptical or Nigella sativa seeds for **asthma**/allergy therapy that targets T-lymphocytes and/or eosinophils
INVENTOR(S): Nassief, Nida Abdul-Ghani
PATENT ASSIGNEE(S): Al-Jassim, Rawaa, Australia; Al-Kaisi, Ban; James, David
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051580	A2	20000908	WO 2000-IB222	20000302
WO 2000051580	A3	20011018		

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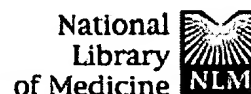
CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
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 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 GB 2348132 A1 20000927 GB 2000-5003 20000301
 EP 1242102 A2 20020925 EP 2000-909548 20000302
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY
 US 2002061841 A1 20020523 US 2001-944564 20010904
 PRIORITY APPLN. INFO.: GB 1999-4777 A 19990302
 GB 1999-13341 A 19990608
 WO 2000-IB222 W 20000302

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 caused by type I hypersensitivity reactions consisting essentially of
 glycoposphopeptical, or pure *Nigella Sativa* seeds, in a concn. which
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 airway inflammation. A method of treatment of allergy using Th1
 stimulating agents, to be administered to a mammal such as human in need
 of such treatment in a shot of 5 days only, resulted in significant
 decrease in symptom score started day 3, and in sputum eosinophils by day
 14, followed by long-term clin. remission of a mean of 6 mo. The BCG-like
 Th1 stimulation is also used in treating diseases in which the body
 defensive mechanism is a cell-mediated immunity, including viral
 infections, including influenza and common cold, chronic and recurrent
 urinary tract infection, pelvic inflammatory diseases as neuroimmune
 appendicitis, cancer, Crohn's disease and facial palsy.

L7 ANSWER 3 OF 3 MEDLINE
 ACCESSION NUMBER: 92377675 MEDLINE
 DOCUMENT NUMBER: 92377675 PubMed ID: 1509986
 TITLE: [Immunologic clinical evaluation of a biological response
 modifier, AM3, in the treatment of childhood infectious
 respiratory pathology].
 Valoracion clinica inmunologica de un modificador de la
 respuesta biologica, AM3, en el tratamiento de la patologia
 respiratoria infecciosa infantil.
 AUTHOR: Sanchez Palacios A; Garcia Marrero J A; Schamann F
 CORPORATE SOURCE: Servicio de Alergologia, Hospital Insular, Las Palmas.
 SOURCE: ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1992 Jan-Feb) 20 (1)
 35-9.
 Journal code: 0370073. ISSN: 0301-0546.
 PUB. COUNTRY: Spain
 DOCUMENT TYPE: (CLINICAL TRIAL)
 (CONTROLLED CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: Spanish
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199209
 ENTRY DATE: Entered STN: 19921009
 Last Updated on STN: 19980206
 Entered Medline: 19920918

AB To assess the immunoclinical effectiveness of a biological response
 immunomodulator, we used AM3 (glycoposphopeptide), a glucomannan
 polysaccharide extracted from the cell wall of a strain of *Candida utilis*,
 in 20 children with asthmatic bronchitis. They received 2 envelopes (1 g)
 daily for 4 months. The results were compared with a control group of 20
 untreated children with the same pathology. The following clinical and
 immunological parameters were assessed in all of them: cough, dyspnea,
 expectoration, frequency and intensity of the bronchospasm, time of
 administration of the symptomatic medication, and the delayed cutaneous

cells response by means of the intradermal reaction of 5 antigens (Trichophyton, Candida albicans, tuberculin, E. coli and bacterial antigens). In the treated group, the immunoferon (AM3) reduced the symptoms, the intensity and frequency of the bronchospasm, and the symptomatic medication (table I, II and III). In basal conditions, the 40 children presented a state of 75% anergy; after 4 months of treatment, the treated group experienced a 45% decrease in their anergic situation, variation which was statistically significant when compared with the control group. In our 20 treated patients, AM3 behaved like and immunostimulant, improving the clinical situation and progress in patients with infectious respiratory disorders. We consider that the immunoferon constitutes a coadjuvant therapy to bacterial immunotherapy.



PubMed	Nucleotide	Protein	Genome	Structure	PMC	Taxonomy	OMIM	Bo
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- ☐ **1:** Gallego Olivella J, Fadurdo Torrus E. Related Article
Study of the immunostimulating effect of glycoposphopeptical (AM3) in mice.
FEMS Immunol Med Microbiol. 1997 May;18(1):87-9.
PMID: 9215591 [PubMed - indexed for MEDLINE]

PubMed Services

- ☐ **2:** Marcos Sanchez F, Juarez Ucelay F, Ramos de Diego MP, Duran Perez-Navarro D. Related Article
[Glycoposphopeptical in the treatment of recurrent oral aphthosis]
An Med Interna. 1994 Jan;11(1):44. Spanish. No abstract available.
PMID: 8025195 [PubMed - indexed for MEDLINE]

Related Resources

- ☐ **3:** Sanchez Palacios A, Garcia Marrero JA, Schamann F. Related Article
[Immunologic clinical evaluation of a biological response modifier, AM3, in treatment of childhood infectious respiratory pathology]
Allergol Immunopathol (Madr). 1992 Jan-Feb;20(1):35-9. Spanish.
PMID: 1509986 [PubMed - indexed for MEDLINE]

- ☐ **4:** Gillissen G, Breuer-Werle M, Schmitz AE. Related Article
[Effects of Immunoferon on humoral immune response]
Rev Clin Esp. 1984 Jan 15;172(1):21-2. Spanish. No abstract available.
PMID: 6709942 [PubMed - indexed for MEDLINE]

- ☐ **5:** Rodriguez F, Brieva A, Tuduri P, Velasco R, Martinez A, Rodriguez-Novas G, Guerrero A, Pivel JP, Sada G. Related Article
[Effect of a new drug on the immune system and its relation to induced infection in the mouse]
Rev Clin Esp. 1983 May 15;169(3):191-3. Spanish. No abstract available.
PMID: 6351183 [PubMed - indexed for MEDLINE]

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Record: 1

Title: Identification and characterization of the peptidic component of the immunomodulatory glycoconjugate Immunoferon.

Author(s): Varela J; Navarro Pico ML; Guerrero A; García F; Giménez Gallego G; Pivel JP

Author's Address: Centro de Investigaciones Biológicas (CIB), Industrial Farmacéutica Cantabria S.A., Madrid, Spain.

Source: Methods and findings in experimental and clinical pharmacology [Methods Find Exp Clin Pharmacol] 2002 Oct; 24 (8), pp. 471-80.

Pub. Type: Journal Article

Language: English

Journal Info: *Country of Publication:* Spain *NLM ID:* 7909595 *ISSN:* 0379-0355 *Subsets:* PreMEDLINE-In Process; IM

Abstract: Immunoferon is a glycoconjugate of natural origin, formed by the noncovalent association of a protein from *Ricinus communis* and a polysaccharidic moiety, and endowed with immunomodulatory as well as pharmacological activities. This study investigated the nature of polypeptidic component of Immunoferon. Through biochemical procedures and comparison with protein databases, the isolated protein was identified as the processed form of the seed of *Ricinus communis* 2S storage polypeptide, which has been termed RicC3. Further analysis of the isolated protein has revealed that it is composed of two different subunits, alpha and beta, which form an heterodimer of high stability and resistance to denaturation, acidic pH and proteolytic cleavage. These findings confirm the excellent properties of the product after oral administration and provide additional support for the pharmacological activities of Immunoferon.

Entry Date(s): *Date Created:* 20021225

Citation ID(s): *PMID:* 12500425 *Medline UI:* 22388841

Database: MEDLINE

Record: 2

Title: AM3 (Immunoférón) as an adjuvant to hepatitis B vaccination in hemodialysis patients.

Author(s): Pérez-García R; Pérez-García A; Verbeelen D; Bernstein ED; Villarrubia VG; Alvarez-Mon M

Author's Address: Nephrology Service, Gregorio Marañón Hospital, Madrid, Spain.

Source: Kidney international [Kidney Int] 2002 May; 61 (5), pp. 1845-52.

Pub. Type: Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial

Language: English

Journal Info: *Country of Publication:* United States *NLM ID:* 0323470 *ISSN:* 0085-2538 *Subsets:* IM

MeSH Terms: Renal Dialysis*
Adjuvants, Immunologic/*administration & dosage
Calcium Phosphates/*administration & dosage
Glycopeptides/*administration & dosage
Hepatitis B Vaccines/*administration & dosage
Hepatitis B, Chronic/*prevention & control
Aged; Double-Blind Method; Female; Follow-Up Studies; Hepatitis B Antibodies/blood; Hepatitis B, Chronic/immunology; Human; Kidney Failure, Chronic/immunology; Kidney Failure, Chronic/therapy; Kidney Failure, Chronic/virology; Male; Middle Age

Abstract: BACKGROUND: Patients with end-stage renal disease (ESRD) undergoing hemodialysis have severe alterations in cell-mediated immunity (CMI) that increases their risk of contracting chronic hepatitis B virus (HBV) infection and decreases their protective responses to HBV vaccine. In an effort to improve the humoral response to an accelerated HBV vaccine protocol in these patients, the ability of an immunomodulator, AM3, to improve seroconversion was investigated. METHODS: A total of 269 patients were enrolled in a multicenter trial. All patients received a DNA recombinant vaccine (40 microg HBsAg/dose/day) on days 0, 10, 21, and 90. AM3 or placebo (3 g/day) was given orally for 30 consecutive days beginning 15 days prior to the first vaccine dose. Anti-HBsAg titers were measured on days 120 and 270 after the beginning of the trial. RESULTS: After one month, 207 patients could be evaluated and 132 patients after six months. The placebo and AM3-treated groups had comparable seroconversion and protective response rates one month after the final vaccine dose. The AM3 treatment group, but not the placebo group, maintained these protective titers up to six months after the final vaccine dose. At this time, the percentage of high responders (anti-HBsAg > 100 IU/L) and mean anti-HBsAg titers in the AM3 group was significantly higher than in the placebo group. CONCLUSIONS: AM3 is a safe and easily tolerated oral agent that potentiates long-term serological immunity to hepatitis B in hemodialysis patients after vaccination.

CAS Registry No.: 0 (Adjuvants, Immunologic)
0 (Calcium Phosphates)
0 (Glycopeptides)
0 (Hepatitis B Antibodies)
0 (Hepatitis B Vaccines)
87139-86-4 (Immunoférón)

Entry Date(s): *Date Created:* 20020422 *Date Completed:* 20021028

Citation ID(s): *PMID:* 11967036 *Medline UI:* 21964541

Database: MEDLINE

Record: 3

Title: Immunoferon, a glycoconjugate of natural origin, inhibits LPS-induced TNF-alpha production and inflammatory responses.

Author(s): Brieva A; Guerrero A; Alonso-Lebrero JL; Pivel JP

Author's Address: R&D Department, Industrial Farmaceutica Cantabria SA, Madrid, Spain.

Source: International immunopharmacology [Int Immunopharmacol] 2001 Oct; 1 (11), pp. 1979-87.

Pub. Type: Journal Article

Language: English

Journal Info: *Country of Publication:* Netherlands *NLM ID:* 100965259 *ISSN:* 1567-5769 *Subsets:* IM

MeSH Terms: Adjuvants, Immunologic/*pharmacology
Anti-Inflammatory Agents, Non-Steroidal/*pharmacology
Calcium Phosphates/*pharmacology
Glycopeptides/*pharmacology
Lipopolysaccharides/*antagonists & inhibitors
Tumor Necrosis Factor/*biosynthesis
Animal; Chromatography, Gas; Corticosterone/blood; Enzyme-Linked Immunosorbent Assay; Indicators and Reagents; Inflammation/pathology; Inflammation/prevention & control; Interleukin-6/biosynthesis; Leukocyte Count; Lipopolysaccharides/metabolism; Lipopolysaccharides/pharmacology; Macrophages, Peritoneal/drug effects; Macrophages, Peritoneal/metabolism; Male; Mice; Mice, Inbred BALB C; Rats; Rats, Inbred Lew

Abstract: We have analyzed the effect of a patented glycoconjugate (GC) of natural origin, Immunoferon, in the development of the response to endotoxemia induced by administration of LPS in rodents. We have observed that oral treatment with the drug reduced the levels of serum TNF-alpha induced by an intravenous pulse of LPS. The serum of pretreated mice blocked TNF-alpha production by peritoneal macrophages. The drug increased the levels of TNF-alpha regulators such as IL-10 and corticosteroids, whereas it inhibited TNF-alpha-dependent IL-6 production. Further TNF-alpha-dependent responses, such as cell extravasation, was decreased in treated mice. According to these results, Immunoferon is postulated as an inhibitor of the systemic response to LPS. Correlation of the observations made in mice with a rat model suggests the efficacy of this product in reducing TNF-alpha production in a species-independent fashion and opens the possibility of its trial as an adjuvant of antibiotics in treatment against gram-negative bacterial infection.

CAS Registry No.: 0 (Adjuvants, Immunologic)
0 (Anti-Inflammatory Agents, Non-Steroidal)
0 (Calcium Phosphates)
0 (Glycopeptides)
0 (Indicators and Reagents)
0 (Interleukin-6)
0 (Lipopolysaccharides)
0 (Tumor Necrosis Factor)
50-22-6 (Corticosterone)
87139-86-4 (Immunoferon)

Entry Date(s): *Date Created:* 20011018 *Date Completed:* 20020322

Citation ID(s): *PMID:* 11606029 *Medline UI:* 21517699

Database: MEDLINE

Record: 4

Title: Immunorestorative effect of thymostimulin on surgery immunodepression: experimental model.

Author(s): Garcia-Lechuz JM; Navarro M; Morandeira MJ; Soria J; Román A; Güemes A; Salinas JC; Lozano R

Author's Address: Department of Surgery, University of Zaragoza, Spain.

Source: European surgical research. Europäische chirurgische Forschung. Recherches chirurgicales europeennes [Eur Surg Res] 1993 Mar-Apr; 25 (2), pp. 74-82.

Pub. Type: Journal Article

Language: English

Journal Info: *Country of Publication:* SWITZERLAND *NLM ID:* 0174752 *ISSN:* 0014-312X *Subsets:* IM; X

MeSH Terms: Surgical Procedures, Operative*
Adjuvants, Immunologic/*pharmacology
Immune Tolerance/*drug effects
Thymus Extracts/*pharmacology
Animal; CD4-CD8 Ratio; Calcium Phosphates/pharmacology; Glycopeptides/pharmacology; Graft Rejection; Lymphocyte Subsets/immunology; Rats; Rats, Inbred WF; Skin Transplantation; Spleen/immunology; Support, Non-U.S. Gov't

Abstract: The purpose of the present study is to ascertain the immunorestorative effect of two different drugs on immunodepression induced by small bowel surgical resection in an experimental model. The potential immunorestorative effect has been measured by the ability of the drug to avoid the delay of skin allograft rejection induced by surgery and the inhibition of CD4/CD8 index changes induced by surgery in spleen tissue. 120 Wistar-Furth rats (age 12-16 weeks) anesthetized with a single intramuscular dose of ketamine (25 mg), diazepam (4 mg) and atropine (0.1 mg) were allotted to two main groups. One group received a skin graft (SG) from Fisher 344 rats and was treated with placebo, Immuferon (AM-3 polypeptidic drug) or TP-1 (thymostimulin) before the experiment (groups I, II, III) or treated with placebo, Immuferon or TP-1 before the experiment and underwent enterectomy and anastomosis (groups IV, V, VI). On the 2nd, 5th and 8th postoperative days, biopsies of the SG were taken and the signs of rejection were microscopically studied and evaluated by a pathologist as zero, incipient, moderate or massive. The other group was treated similarly, but the animals did not receive a SG and were splenectomized 5 days later. CD4 and CD8 lymphocyte subpopulations were identified by means of immunoperoxidase technique and monoclonal antibodies. Thymostimulin is able to stimulate the presence of SG rejection signs on the 2nd postoperative day in nonenterectomized animals and on the 8th postoperative day in nonenterectomized animals and on the 8th postoperative day in enterectomized rats and is able to avoid the decrease of the CD4/CD8 index in spleen tissue after surgical immunodepression.(ABSTRACT TRUNCATED AT 250 WORDS)

CAS Registry No.: 0 (Adjuvants, Immunologic)
0 (Calcium Phosphates)
0 (Glycopeptides)
0 (Thymus Extracts)
0 (thymostimulin)
87139-86-4 (Immuferon)

Revision Date: 20011113

Entry Date(s): *Date Created:* 19930602 *Date Completed:* 19930602

Citation ID(s): *PMID:* 8482312 *Medline UI:* 93245837

Database: MEDLINE

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Author's Address: Centro de Investigaciones Biológicas (CIB), Industrial Farmacéutica Cantabria S.A., Madrid, Spain.

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Language: English

Journal Info: *Country of Publication:* Spain *NLM ID:* 7909595 *ISSN:* 0379-0355 *Subsets:* PreMEDLINE-In Process; IM

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Author's Address: Nephrology Service, Gregorio Marañón Hospital, Madrid, Spain.
Source: Kidney international [Kidney Int] 2002 May; 61 (5), pp. 1845-52.
Pub. Type: Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial
Language: English
Journal Info: *Country of Publication:* United States *NLM ID:* 0323470 *ISSN:* 0085-2538 *Subsets:* IM
MeSH Terms: Renal Dialysis*
Adjuvants, Immunologic/*administration & dosage
Calcium Phosphates/*administration & dosage
Glycopeptides/*administration & dosage
Hepatitis B Vaccines/*administration & dosage
Hepatitis B, Chronic/*prevention & control
Aged; Double-Blind Method; Female; Follow-Up Studies; Hepatitis B Antibodies/blood; Hepatitis B, Chronic/immunology; Human; Kidney Failure, Chronic/immunology; Kidney Failure, Chronic/therapy; Kidney Failure, Chronic/virology; Male; Middle Age

Abstract: BACKGROUND: Patients with end-stage renal disease (ESRD) undergoing hemodialysis have severe alterations in cell-mediated immunity (CMI) that increases their risk of contracting chronic hepatitis B virus (HBV) infection and decreases their protective responses to HBV vaccine. In an effort to improve the humoral response to an accelerated HBV vaccine protocol in these patients, the ability of an immunomodulator, AM3, to improve seroconversion was investigated. METHODS: A total of 269 patients were enrolled in a multicenter trial. All patients received a DNA recombinant vaccine (40 microg HBsAg/dose/day) on days 0, 10, 21, and 90. AM3 or placebo (3 g/day) was given orally for 30 consecutive days beginning 15 days prior to the first vaccine dose. Anti-HBsAg titers were measured on days 120 and 270 after the beginning of the trial. RESULTS: After one month, 207 patients could be evaluated and 132 patients after six months. The placebo and AM3-treated groups had comparable seroconversion and protective response rates one month after the final vaccine dose. The AM3 treatment group, but not the placebo group, maintained these protective titers up to six months after the final vaccine dose. At this time, the percentage of high responders (anti-HBsAg > 100 IU/L) and mean anti-HBsAg titers in the AM3 group was significantly higher than in the placebo group. CONCLUSIONS: AM3 is a safe and easily tolerated oral agent that potentiates long-term serological immunity to hepatitis B in hemodialysis patients after vaccination.

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87139-86-4 (Immuferon)

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Lipopolysaccharides/*antagonists & inhibitors
Tumor Necrosis Factor/*biosynthesis
Animal; Chromatography, Gas; Corticosterone/blood; Enzyme-Linked Immunosorbent Assay; Indicators and Reagents; Inflammation/pathology; Inflammation/prevention & control; Interleukin-6/biosynthesis; Leukocyte Count; Lipopolysaccharides/metabolism; Lipopolysaccharides/pharmacology; Macrophages, Peritoneal/drug effects; Macrophages, Peritoneal/metabolism; Male; Mice; Mice, Inbred BALB C; Rats; Rats, Inbred Lew

Abstract: We have analyzed the effect of a patented glycoconjugate (GC) of natural origin, Immuferon, in the development of the response to endotoxemia induced by administration of LPS in rodents. We have observed that oral treatment with the drug reduced the levels of serum TNF-alpha induced by an intravenous pulse of LPS. The serum of pretreated mice blocked TNF-alpha production by peritoneal macrophages. The drug increased the levels of TNF-alpha regulators such as IL-10 and corticosteroids, whereas it inhibited TNF-alpha-dependent IL-6 production. Further TNF-alpha-dependent responses, such as cell extravasation, was decreased in treated mice. According to these results, Immuferon is postulated as an inhibitor of the systemic response to LPS. Correlation of the observations made in mice with a rat model suggests the efficacy of this product in reducing TNF-alpha production in a species-independent fashion and opens the possibility of its trial as an adjuvant of antibiotics in treatment against gram-negative bacterial infection.

CAS Registry No.: 0 (Adjuvants, Immunologic)
0 (Anti-Inflammatory Agents, Non-Steroidal)
0 (Calcium Phosphates)
0 (Glycopeptides)
0 (Indicators and Reagents)
0 (Interleukin-6)
0 (Lipopolysaccharides)
0 (Tumor Necrosis Factor)
50-22-6 (Corticosterone)
87139-86-4 (Immuferon)

Entry Date(s): *Date Created:* 20011018 *Date Completed:* 20020322

Citation ID(s): *PMID:* 11606029 *Medline UI:* 21517699

Database: MEDLINE

Record: 4

Title: Immunorestorative effect of thymostimulin on surgery immunodepression: experimental model.

Author(s): García-Lechuz JM; Navarro M; Morandeira MJ; Soria J; Román A; Güemes A; Salinas JC; Lozano R

Author's Address: Department of Surgery, University of Zaragoza, Spain.

Source: European surgical research. Europäische chirurgische Forschung. Recherches chirurgicales europeennes [Eur Surg Res] 1993 Mar-Apr; 25 (2), pp. 74-82.

Pub. Type: Journal Article

Language: English

Journal Info: *Country of Publication:* SWITZERLAND *NLM ID:* 0174752 *ISSN:* 0014-312X *Subsets:* IM; X

MeSH Terms: Surgical Procedures, Operative*
Adjuvants, Immunologic/*pharmacology
Immune Tolerance/*drug effects
Thymus Extracts/*pharmacology
Animal; CD4-CD8 Ratio; Calcium Phosphates/pharmacology; Glycopeptides/pharmacology; Graft Rejection; Lymphocyte Subsets/immunology; Rats; Rats, Inbred WF; Skin Transplantation; Spleen/immunology; Support, Non-U.S. Gov't

Abstract: The purpose of the present study is to ascertain the immunorestorative effect of two different drugs on immunodepression induced by small bowel surgical resection in an experimental model. The potential immunorestorative effect has been measured by the ability of the drug to avoid the delay of skin allograft rejection induced by surgery and the inhibition of CD4/CD8 index changes induced by surgery in spleen tissue. 120 Wistar-Furth rats (age 12-16 weeks) anesthetized with a single intramuscular dose of ketamine (25 mg), diazepam (4 mg) and atropine (0.1 mg) were allotted to two main groups. One group received a skin graft (SG) from Fisher 344 rats and was treated with placebo, Immuferon (AM-3 polypeptidic drug) or TP-1 (thymostimulin) before the experiment (groups I, II, III) or treated with placebo, Immuferon or TP-1 before the experiment and underwent enterectomy and anastomosis (groups IV, V, VI). On the 2nd, 5th and 8th postoperative days, biopsies of the SG were taken and the signs of rejection were microscopically studied and evaluated by a pathologist as zero, incipient, moderate or massive. The other group was treated similarly, but the animals did not receive a SG and were splenectomized 5 days later. CD4 and CD8 lymphocyte subpopulations were identified by means of immunoperoxidase technique and monoclonal antibodies. Thymostimulin is able to stimulate the presence of SG rejection signs on the 2nd postoperative day in nonenterectomized animals and on the 8th postoperative day in nonenterectomized animals and on the 8th postoperative day in enterectomized rats and is able to avoid the decrease of the CD4/CD8 index in spleen tissue after surgical immunodepression.(ABSTRACT TRUNCATED AT 250 WORDS)

CAS Registry No.: 0 (Adjuvants, Immunologic)
0 (Calcium Phosphates)
0 (Glycopeptides)
0 (Thymus Extracts)
0 (thymostimulin)
87139-86-4 (Immuferon)

Revision Date: 20011113

Entry Date(s): *Date Created:* 19930602 *Date Completed:* 19930602

Citation ID(s): *PMID:* 8482312 *Medline UI:* 93245837

Database: MEDLINE

Record: 5

Title: [The clinical evaluation of glycoposphopeptical (Immunoferon) as combined treatment in patients with chronic lung disease]

Transliterated Title: Valoración clínica de glicofosfopeptical (Immunoferon) como tratamiento asociado en pacientes afectos de enfermedad pulmonar crónica.

Author(s): Marcos Sánchez F; Rodríguez Gallego C; Celdrán Gil J; Durán Pérez-Navarro A

Source: Anales de medicina interna : organo oficial de la Sociedad Espanola de Medicina Interna [An Med Interna] 1989 Dec; 6 (12), pp. 657-8.

Pub. Type: Letter

Language: Spanish

Journal Info: *Country of Publication:* SPAIN *NLM ID:* 9112183 *ISSN:* 0212-7199 *Subsets:* IM

MeSH Terms: Calcium Phosphates/*therapeutic use
Glycopeptides/*therapeutic use
Lung Diseases, Obstructive/*drug therapy
Aged; Drug Evaluation; Drug Therapy, Combination; Female; Human; Male; Middle Age

CAS Registry No.: 0 (Calcium Phosphates)
0 (Glycopeptides)
87139-86-4 (Immunoferon)

Revision Date: 20001218

Entry Date(s): *Date Created:* 19911016 *Date Completed:* 19911016

Citation ID(s): *PMID:* 2491481 *Medline UI:* 91363626

Database: MEDLINE

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L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:223217 CAPLUS

DOCUMENT NUMBER: 136:334953

TITLE: Compilation and meta-analysis of randomized placebo-controlled clinical trials on the prevention of **respiratory** tract infections in children using immunostimulants

AUTHOR(S): Berber, Arturo; Del-Rio-Navarro, Blanca

CORPORATE SOURCE: Allergy and Immunology Service, Hospital Infantil de Mexico "Federico Gomez," Mexico City, Mex.

SOURCE: Journal of Investigational Allergology and Clinical Immunology (2001), 11(4), 235-246

CODEN: JIAIEF; ISSN: 1018-9068

PUBLISHER: Hogrefe & Huber Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several immunostimulants presume to prevent **respiratory** tract infections (RTIs) in children, but their efficacy is controversial. Aim was to compile the findings of the randomized, placebo-controlled trials (RCTs) on the prevention of acute **respiratory** tract infections (ARTIs) in children using immunostimulants, and to perform a meta-anal. Medline, EMBASE databases, and register of Cochrane Acute **Respiratory** Infection Group. We searched all the refs. of immunostimulants and selected papers referring to RCTs on the prevention of ARTIs in children. Papers were rated according to Jadad's instrument. We abstracted the no. of ARTIs, and a one-tailed probability value (p) was abstracted for each trial. Effect of medication was detd. as weighted mean \pm SE of percent redn. of ARTIs regarding ARTIs of placebo groups as 100%. Four of five RCTs with Jadad's score > 3 showed significant redn. of ARTIs in immunostimulant groups. When only the trials reporting mean \pm SD and/or dispersion were considered (n = 16), the global weighted percent effect of immunostimulants showed a change of -42.64%, with 95% confidence intervals from -45.19% to -40.08%; i.e., the treated group presented about 60% of the mean no. of ARTIs in the placebo group. According to this meta-anal. and RCTs with Jadad's score > 3 , immunostimulants are an effective treatment for the prevention of ARTI. Further high-quality RCTs are required to demonstrate the effect and the size of the effect of each individual immunostimulant.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Compilation and meta-analysis of randomized placebo-controlled clinical trials on the prevention of **respiratory** tract infections in children using immunostimulants

AB Several immunostimulants presume to prevent **respiratory** tract infections (RTIs) in children, but their efficacy is controversial. Aim was to compile the findings of the randomized, placebo-controlled trials (RCTs) on the prevention of acute **respiratory** tract infections (ARTIs) in children using immunostimulants, and to perform a meta-anal. Medline, EMBASE databases, and register of Cochrane Acute **Respiratory** Infection Group. We searched all the refs. of immunostimulants and selected papers referring to RCTs on the prevention of ARTIs in children. Papers were rated according to Jadad's instrument. We abstracted the no. of ARTIs, and a one-tailed probability value (p) was abstracted for each trial. Effect of medication was detd. as weighted mean \pm SE of percent redn. of ARTIs regarding ARTIs of placebo groups as 100%. Four of five RCTs with Jadad's score > 3 showed significant redn. of ARTIs in immunostimulant groups. When only the trials reporting mean \pm SD and/or dispersion were considered (n = 16), the global weighted percent effect of immunostimulants showed a change of -42.64%, with 95% confidence intervals from -45.19% to -40.08%; i.e., the treated group presented about 60% of the mean no. of ARTIs in the placebo group. According to this meta-anal. and RCTs with Jadad's score > 3 , immunostimulants are an effective treatment for the prevention of ARTI. Further high-quality RCTs are required to demonstrate the effect and the

size of the effect of each individual immunostimulant.

ST immunostimulant **respiratory** tract infection child meta analysis

IT Pelargonium sidoides
(Umckaloabo; immunostimulants in prevention of **respiratory**
tract infections in children (meta-anal.))

IT Development, mammalian postnatal
(child; immunostimulants in prevention of **respiratory** tract
infections in children (meta-anal.))

IT Human
Immunostimulants
Ribosome
(immunostimulants in prevention of **respiratory** tract
infections in children (meta-anal.))

IT Thymus hormones
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(immunostimulants in prevention of **respiratory** tract
infections in children (meta-anal.))

IT **Respiratory** tract
(infection; immunostimulants in prevention of **respiratory**
tract infections in children (meta-anal.))

IT Information systems
(searching; immunostimulants in prevention of **respiratory**
tract infections in children (meta-anal.))

IT **87139-86-4**, Immuferon 88402-38-4, Broncho-Vaxom 121808-62-6,
Adimod 123243-05-0, Paspal 146418-27-1, Biostim 153191-77-6, Luivac
419574-57-5, Immunobalt 419574-58-6, Munostin 419574-59-7, Pulmonar OM
419574-60-0, Ribovac 419574-61-1, Immucytal
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(immunostimulants in prevention of **respiratory** tract
infections in children (meta-anal.))

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:627968 CAPLUS

DOCUMENT NUMBER: 133:202992

TITLE: Glycophosphopeptical or Nigella sativa seeds for
asthma/allergy therapy that targets
T-lymphocytes and/or eosinophils

INVENTOR(S): Nassief, Nida Abdul-Ghani

PATENT ASSIGNEE(S): Al-Jassim, Rawaa, Australia; Al-Kaisi, Ban; James,
David

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051580	A2	20000908	WO 2000-IB222	20000302
WO 2000051580	A3	20011018		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
GB 2348132	A1	20000927	GB 2000-5003	20000301
EP 1242102	A2	20020925	EP 2000-909548	20000302

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI, CY

US 2002061841 A1 20020523 US 2001-944564 20010904
PRIORITY APPLN. INFO.: GB 1999-4777 A 19990302
GB 1999-13341 A 19990608
WO 2000-1B222 W 20000302

- AB A pharmaceutical compn. for the treatment and/or prophylaxis of diseases caused by type I hypersensitivity reactions consisting essentially of glycoposphopeptical, or pure Nigella Sativa seeds, in a concn. which stimulate Th1 lymphocytes and selectively switch-off the eosinophilic airway inflammation. A method of treatment of **allergy** using Th1 stimulating agents, to be administered to a mammal such as human in need of such treatment in a shot of 5 days only, resulted in significant decrease in symptom score started day 3, and in sputum eosinophils by day 14, followed by long-term clin. remission of a mean of 6 mo. The BCG-like Th1 stimulation is also used in treating diseases in which the body defensive mechanism is a cell-mediated immunity, including viral infections, including influenza and common cold, chronic and recurrent urinary tract infection, pelvic inflammatory diseases as neuroimmune appendicitis, cancer, Crohn's disease and facial palsy.
- TI Glycoposphopeptical or Nigella sativa seeds for **asthma/**
allergy therapy that targets T-lymphocytes and/or eosinophils
- AB A pharmaceutical compn. for the treatment and/or prophylaxis of diseases caused by type I hypersensitivity reactions consisting essentially of glycoposphopeptical, or pure Nigella Sativa seeds, in a concn. which stimulate Th1 lymphocytes and selectively switch-off the eosinophilic airway inflammation. A method of treatment of **allergy** using Th1 stimulating agents, to be administered to a mammal such as human in need of such treatment in a shot of 5 days only, resulted in significant decrease in symptom score started day 3, and in sputum eosinophils by day 14, followed by long-term clin. remission of a mean of 6 mo. The BCG-like Th1 stimulation is also used in treating diseases in which the body defensive mechanism is a cell-mediated immunity, including viral infections, including influenza and common cold, chronic and recurrent urinary tract infection, pelvic inflammatory diseases as neuroimmune appendicitis, cancer, Crohn's disease and facial palsy.
- ST glycoposphopeptical immunostimulant cell mediated immunity;
allergy T cell eosinophil glycoposphopeptical immunostimulant;
asthma T cell eosinophil glycoposphopeptical immunostimulant
- IT Intestine, disease
(Crohn's; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)
- IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(E, type 1 IgE-mediated hypersensitivity; glycoposphopeptical or
Nigella sativa seeds for **asthma/allergy** therapy
targeting t-lymphocytes and/or eosinophils)
- IT Lymphocyte
(activation; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)
- IT Reproductive tract
(adnexitis; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)
- IT Eye, disease
(allergic conjunctivitis; glycoposphopeptical or Nigella sativa seeds
for **asthma/allergy** therapy targeting t-lymphocytes
and/or eosinophils)
- IT Nose
(allergic rhinitis; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or

eosinophils)

IT Dermatitis
(atopic; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Drug delivery systems
(capsules; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Immunity
(cell-mediated; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Urticaria
(chronic; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT **Allergy**
 Asthma
 (diagnosis; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Larynx
(edema; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Cytokines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(eosinophil chemotactic factor; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Paralysis
(facial palsy; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Drugs
(gastrointestinal; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT **Allergy** inhibitors
 Anti-inflammatory agents
 Antiasthmatics
 Antitumor agents
 Antiviral agents
 Common cold
 Drug delivery systems
 Eosinophil
 Immunostimulants
 Influenza
 Mycobacterium BCG
 (glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT T cell (lymphocyte)
(helper cell/inducer, TH1; glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy targeting t-lymphocytes and/or eosinophils)

IT **Allergy**
(immediate hypersensitivity; glycoposphopeptical or Nigella sativa

seeds for **asthma/allergy** therapy targeting
t-lymphocytes and/or eosinophils)

IT **Respiratory** tract
Urinary tract
(infection; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT **Respiratory** tract
(inflammation; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(lozenges; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Cell activation
Cell proliferation
(lymphocyte; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Appendix
(neuroimmune appendicitis; glycoposphopeptical or Nigella sativa seeds
for **asthma/allergy** therapy targeting t-lymphocytes
and/or eosinophils)

IT Drug delivery systems
(ointments, creams; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(ointments; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(powders; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Lymphocyte
(proliferation; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Tuberculin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(purified protein deriv.; glycoposphopeptical or Nigella sativa seeds
for **asthma/allergy** therapy targeting t-lymphocytes
and/or eosinophils)

IT Nose
(rhinitis, perennial; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Nigella sativa
(seeds; glycoposphopeptical or Nigella sativa seeds for **asthma**
/allergy therapy targeting t-lymphocytes and/or eosinophils)

IT Drug delivery systems
(solns., nasal; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(solns., ophthalmic; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(suspensions; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(syrups; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(tablets; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(topical; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT Drug delivery systems
(vaginal; glycoposphopeptical or Nigella sativa seeds for
asthma/allergy therapy targeting t-lymphocytes and/or
eosinophils)

IT **87139-86-4**, Immunoferon
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(glycoposphopeptical or Nigella sativa seeds for **asthma/
allergy** therapy targeting t-lymphocytes and/or eosinophils)

L3 ANSWER 3 OF 7 MEDLINE
ACCESSION NUMBER: 2001404094 MEDLINE
DOCUMENT NUMBER: 21294697 PubMed ID: 11401877
TITLE: Defective natural killer and phagocytic activities in
chronic obstructive pulmonary disease are restored by
glycoposphopeptical (immunoferon).
AUTHOR: Prieto A; Reyes E; Bernstein E D; Martinez B; Monserrat J;
Izquierdo J L; Callol L; de LUCAS P; Alvarez-Sala R;
Alvarez-Sala J L; Villarrubia V G; Alvarez-Mon M
CORPORATE SOURCE: Department of Medicine CSIC Associated Unit, University of
Alcala, Alcala de Henares, Madrid, Spain.
SOURCE: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE,
(2001 Jun) 163 (7) 1578-83.
Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB We have investigated both modifications in natural (innate) immunity
caused by chronic obstructive pulmonary disease (COPD) and the effects of
a glycoposphopeptical immunomodulator (Immunoferon) treatment on
COPD-associated immunoalterations. In a double-blinded clinical trial, 60
patients with COPD received glycoposphopeptical or placebo during 90
consecutive days at oral doses of 3 g/d. Fifty-six sex- and age-matched
healthy control subjects were included as a reference group for
immunologic parameters. Peripheral blood natural killer (PBNK) cell
cytotoxic activity and phagocytic activity of peripheral
monocytes/macrophages (Mo/Ma) and polymorphonuclear (PMN) cells were
assessed at baseline and then again at the end of treatments. We found
both PBNK activity and phagocytic activity to be significantly decreased
in patients with COPD compared with levels in healthy volunteers. The
treatment with glycoposphopeptical provoked significant stimulatory
effects on PBNK cytotoxic activity. This stimulation was not mediated by
an increase in CD3(-)CD56(+) NK cells. Further, glycoposphopeptical
significantly increased the percentage of monocytes and PMNs that

phagocytize Escherichia coli in vitro, as well as increased phagocytic indices. We conclude that peripheral blood cells of patients with COPD show clear defects in natural immunity that are partially rescued by glycophosphopeptical.

CT

Phosphates: TU, therapeutic use
Cytotoxicity, Immunologic: DE, drug effects
Double-Blind Method
*Glycopeptides: TU, therapeutic use
*Killer Cells, Natural: IM, immunology
*Lung Diseases, Obstructive: IM, immunology
Macrophages: IM, immunology
Middle Age
Neutrophils: IM, immunology
*Phagocytosis: DE, drug effects

RN 87139-86-4 (Immunoferon)

L3 ANSWER 4 OF 7 MEDLINE

ACCESSION NUMBER: 92377675 MEDLINE

DOCUMENT NUMBER: 92377675 PubMed ID: 1509986

TITLE: [Immunologic clinical evaluation of a biological response modifier, AM3, in the treatment of childhood infectious respiratory pathology].
Valoracion clinica inmunologica de un modificador de la respuesta biologica, AM3, en el tratamiento de la patologia respiratoria infecciosa infantil.

AUTHOR: Sanchez Palacios A; Garcia Marrero J A; Schamann F
CORPORATE SOURCE: Servicio de Alergologia, Hospital Insular, Las Palmas.
SOURCE: ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1992 Jan-Feb) 20 (1) 35-9.

Journal code: 0370073. ISSN: 0301-0546.

PUB. COUNTRY: Spain

DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Spanish

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199209

ENTRY DATE: Entered STN: 19921009
Last Updated on STN: 19980206
Entered Medline: 19920918

AB To assess the immunoclinical effectiveness of a biological response immunomodulator, we used AM3 (glycophosphopeptide), a glucomannan polysaccharide extracted from the cell wall of a strain of Candida utilis, in 20 children with asthmatic bronchitis. They received 2 envelopes (1 g) daily for 4 months. The results were compared with a control group of 20 untreated children with the same pathology. The following clinical and immunological parameters were assessed in all of them: cough, dyspnea, expectoration, frequency and intensity of the bronchospasm, time of administration of the symptomatic medication, and the delayed cutaneous cells response by means of the intradermal reaction of 5 antigens (Trichophyton, Candida albicans, tuberculin, E. coli and bacterial antigens). In the treated group, the immunoferon (AM3) reduced the symptoms, the intensity and frequency of the bronchospasm, and the symptomatic medication (table I, II and III). In basal conditions, the 40 children presented a state of 75% anergy; after 4 months of treatment, the treated group experienced a 45% decrease in their anergic situation, variation which was statistically significant when compared with the control group. In our 20 treated patients, AM3 behaved like and immunostimulant, improving the clinical situation and progress in patients with infectious respiratory disorders. We consider that the immunoferon constitutes a coadjuvant therapy to bacterial immunotherapy.

TI [Immunologic clinical evaluation of a biological response modifier, AM3, in the treatment of childhood infectious respiratory pathology].

Valoracion clinica inmunologica de un modificador de la respuesta biologica, AM3, en el tratamiento de la patologia respiratoria infecciosa.

AB . . . In our 20 treated patients, AM3 behaved like and immunostimulant, improving the clinical situation and progress in patients with infectious **respiratory** disorders. We consider that the immunoferon constitutes a coadjuvant therapy to bacterial immunotherapy.

CT Check Tags: Human
Antibiotics: TU, therapeutic use
Antitussive Agents: TU, therapeutic use
Asthma: CO, complications
Asthma: TH, therapy
*Biological Response Modifiers: TU, therapeutic use
Bronchial Spasm: CO, complications
Bronchial Spasm: TH, therapy
*Calcium Phosphates: TU, . . . Therapy
Disease Susceptibility
Double-Blind Method
English Abstract
Expectorants: TU, therapeutic use
*Glycopeptides: TU, therapeutic use
Immunity, Cellular
Intradermal Tests
Recurrence
Respiratory Hypersensitivity: CO, complications
Respiratory Hypersensitivity: DT, drug therapy
*Respiratory Hypersensitivity: TH, therapy
Respiratory Tract Infections: CO, complications
Respiratory Tract Infections: DT, drug therapy
*Respiratory Tract Infections: TH, therapy

RN 87139-86-4 (Immunoferon)

L3 ANSWER 5 OF 7 MEDLINE

ACCESSION NUMBER: 91363626 MEDLINE

DOCUMENT NUMBER: 91363626 PubMed ID: 2491481

TITLE: [The clinical evaluation of glycoposphopeptical (Immunoferon) as combined treatment in patients with chronic lung disease].
Valoracion clinica de glicofosfopeptical (Immunoferon) como tratamiento asociado en pacientes afectos de enfermedad pulmonar cronica.

AUTHOR: Marcos Sanchez F; Rodriguez Gallego C; Celdran Gil J; Duran Perez-Navarro A

SOURCE: ANALES DE MEDICINA INTERNA, (1989 Dec) 6 (12) 657-8.
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TI [The clinical evaluation of glycoposphopeptical (Immunoferon) as combined treatment in patients with chronic lung disease].
Valoracion clinica de glicofosfopeptical (Immunoferon) como tratamiento asociado en pacientes afectos de enfermedad pulmonar cronica.

CT . . . Check Tags: Female; Human; Male
Aged

*Calcium Phosphates: TU, therapeutic use
Drug Evaluation
Drug Therapy, Combination

*Glycopeptides: TU, therapeutic use

*Lung Diseases, Obstructive: DT, drug therapy

Middle Age
RN 87139-86-4 (Immunoferon)

L3 ANSWER 6 OF 7 USPATFULL

ACCESSION NUMBER: 2002:119853 USPATFULL

TITLE: **Asthma/allergy** therapy that targets
T-lymphocytes and/or eosinophils

INVENTOR(S): Nassief, Nida Abdul-Ghani, Doha, IRAQ

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002061841	A1	20020523
APPLICATION INFO.:	US 2001-944564	A1	20010904 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-4777	19990302
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	AL-JASSIM, Rawaa, 2578 River Woods Drive, Naperville, IL, 60565	

NUMBER OF CLAIMS: 24

EXEMPLARY CLAIM: 1

LINE COUNT: 772

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition for the treatment and/or prophylaxis of diseases caused by type I hypersensitivity reactions consisting essentially of Glicophosphopeptical, or pure Nigella Sativa seeds, in a concentration which stimulate Th1 lymphocytes and selectively switch-off the eosinophilic airway inflammation

A method of treatment of **allergy** using Th1 stimulating agents, to be administered to a mammal such as human in need of such treatment in a shot of 5 days only, resulted in significant decrease in symptom score started day 3, and in sputum eosinophils by day 14, followed by long-term clinical remission of a mean of 6 months.

The BCG-like Th1 stimulation is also used in treating diseases in which the body defensive mechanism is a Cell Mediated Immunity, including viral infections, as but not limited to influenza and common cold, Chronic and recurrent urinary tract infection, pelvic inflammatory diseases as neuroimmune appendicitis, cancer, crohns disease and facial palsy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Asthma/allergy** therapy that targets T-lymphocytes and/or eosinophils

AB A method of treatment of **allergy** using Th1 stimulating agents, to be administered to a mammal such as human in need of such treatment in a . . .

SUMM . . . generally directed to the fields of medicine and pharmacology, and specifically directed to a pharmaceutical composition for the treatment of **asthma/allergy**, consisting essentially of Glycosphosphopeptical, or as an equivalent pure Nigella sativa seeds, which is active to stimulate T-helper lymphocytes type 1 therefor selectively switching-off the eosinophilic inflammation, also treating viral **respiratory** tract infections (flue & influenza), other viral infection, urinary tract infection, pelvic inflammatory diseases in particular neuroimmune appendicitis, cancer, crohns. . .

SUMM [0003] **Asthma** is the epidemic of the new millennium. Despite the increase in our knowledge, the morbidity, mortality and prevalence of **asthma** and other allergic diseases are increasing as shown by WHO statistics. (1)

SUMM [0004] Barnes J December 1999, review the current state of anti-

asthma therapy, over the past 10 years there have been striking improvement in the treatment of **asthma** largely as a result of the earlier and more widespread use of inhaled corticosteroids. The developments of new treatments for **asthma** has proved difficult, although several immunologic approaches are undergoing preclinical and clinical assessment. Antileukotrienes are the only new class of drugs to treat **asthma** that have been introduced in the past 25 years, but their efficacy is somewhat limited and unpredictable, as compared with. . .

- SUMM . . . was not associated with large reductions in markers of eosinophilic inflammation, bronchovascular permeability, or mucus hypersecretion. Alternative therapies for corticosteroid-dependant **asthma**, such as methotrexate, cyclosporine and oral gold, are problematic and have high incidence of adverse effect. (2)
- SUMM . . . accordingly an outstanding need for an effective and convenient means for treating and/or preventing type I IgE-mediated hypersensitivity reactions, including **asthma**, in mammals.
- SUMM [0008] Glycophosphopeptical: The present inventor has, surprisingly, found that a short-term administration of Glycophosphopeptical (Glicofosfopeptical) to patients suffering from **asthma** is capable of treating and/or preventing **asthma**, Glycophosphopeptical is marketed under the trade names "IMMUNOFERON" and "IMMUNOFERON" drug by Industrial Farmaceutica Cantabria, S.A. (Spain), Glycophosphopeptical is a . . . and stimulating cell mediated immunity. It is not indicated for the treatment of diseases caused by type I hypersensitivity and **asthma** defined
- SUMM . . . widely available for use as a spice or condiment. *Nigella sativa* is folk medicines, treating many diseases including many with **respiratory** symptoms.
- SUMM [0019] The following studies are considered relevant to the relation between *N. sativa* and **asthma** Sayed 1980: The oil is used in the treatment of **asthma**, **respiratory** oppression and coughs. The active principal, nigellone, has been isolated from the volatile oil fraction and is reported to be useful in the treatment of bronchial **asthma**. (9)
- SUMM [0021] El-Tahir et al 1993: The **respiratory** effect of the volatile oil of the black seed (*Nigella sativa*) in guinea-pig: elucidation of the mechanism (s) of action.. . .
- SUMM . . . immunity to tuberculosis by stimulating Cell Mediated Immunity mediated by T lymphocytes (Th1). The relation of BCG vaccination to **asthma** is a debate. BCG has also been used as a therapeutic agent in the treatment of cancer, inducing Cell Mediated. . .
- SUMM [0029] Currently, IgE production is under the control of Interleukins produced by T-helper 2 lymphocyte, **allergy** is clearly a Th2 disease.
- SUMM [0031] **Asthma** is an inflammatory mediator soup. (21)
- SUMM [0033] 5- My novel concept in immunopathology of **allergy**
- SUMM [0034] A normal person is in a state of "Tolerance to Environmental Antigen, TEA". Pre-inflammatory phase of **allergy** is controlled by Th1 cells, and it's cytokine interferon. This is based on my discovery that interferon is a potent. . .
- SUMM [0035] Th1 suppression is the cause of **allergy**. Manifested by low serum interferon in acute asthmatic attacks. (26, 27)
- SUMM . . . of selectively switch-off the eosinophilic airway inflammation, normalizing serum interferon This can be achieved by using a novel class of **asthma** therapy, which is the subject of this invention. "days" therapy with a BCG-like Th1 stimulation .fwdarw. long term clinical remission
- SUMM [0037] The present invention is introducing a new class of anti-**allergy/anti-asthma** therapy that target the pre-inflammatory phase of the allergic reaction being defined by the present inventor as "Th1 lymphocytes" and. . .
- SUMM [0038] This present invention provides a pharmaceutical composition and treatment of **asthma/allergy**, consisting essentially

of Glycophosphopeptical, or an equivalent pure *Nigella sativa* seeds, which is active to stimulate T-helper lymphocytes type I. . .

SUMM [0039] The present inventor has, surprisingly, provided a method of treatment for patients suffering from **asthma/allergy**, administering Glycophosphopeptical to a mammal such as human in need of such treatment a shot of 5 days only, to. . .

SUMM . . . for the treatment and/or prophylaxis of diseases caused by type I IgE-mediated hypersensitivity reaction, such as extrinsic, intrinsic or mixed **asthma**, allergic and perennial rhinitis, allergic conjunctivitis, chronic urticaria, atopic dermatitis, and/or laryngeal oedema, to be administered to a mammal such. . .

SUMM [0046] The use of Th1 stimulating agents in the treatment of **allergy/asthma** is dependent on the fact that interferon is an in vivo Eosinophilic Chemotactic Factor, and that serum interferon and Th1. . .

SUMM [0047] The method of treating a chronic **asthma** and **allergy** using 5 days schedule is based on that the recommended dose of Th1 lymphocytes stimulating agent is sufficient to selectively. . .

SUMM . . . for the treatment and/or prophylaxis of diseases characterized by a body immune defensive mechanism is Cell Mediated Immunity as viral **respiratory** tract infections such as, but not limited to influenza and common cold, other viral infections. . .

SUMM [0050] Additionally the present invention provide a method of treatment of viral **respiratory** tract infections such as, but not limited to influenza and common cold, other viral infections comprising the administration to a. . .

SUMM . . . 1-20 days, preferably 5 days for type 1 hypersensitivity reaction, of particular interest but not limited to the chronic corticosteroid-dependent **allergy** and **asthma**. It provides a steroid saving activity.

SUMM [0057] Manufacturing a pharmaceutical preparation to provide a therapy for mammals including humans for the treatment of **asthma** and **allergy**, also a Th1 stimulating and Cell Mediated Immunity stimulating remedy for viral diseases urinary tract infection, pelvic inflammatory disease, crohns. . .

DETD . . . invention was conceived during October 1993, after an experiment of nature that happened to the inventor. Being sever asthmatic her **asthma** was relived after certain health incident. As an immunologist she linked the incident with interferon. This is considered as Stage. . . Chemotactic Factor. Stage III: A marketed drug immunoferon (glycophosphopeptical), indicated for diseases unrelated to type 1 hypersensitivity, was linked with **allergy** in a novel way (depending on the above observation), using it in a non-routine indication and dosage.

DETD . . . its utility and reduction to practice, a double-blind placebo controlled clinical trial was designed. 120 subjects with different types of **allergy** were chosen and divided into two groups, matched for age, sex, and severity of the allergic condition after an informed. . .

DETD [0060] 1 - Diseases involved include seasonal allergic rhinitis, allergic conjunctivitis, chronic urticaria, **asthma**, and laryngeal edema.

DETD . . . treatment, the total dose received and the schedule of therapy were verified to find the best method of treating various **allergies**. Glycophosphopeptical was given in addition to the conventional therapy. The full course of 15 g total dose, was divided over. . .

DETD [0076] **Asthma**: dyspnoea, wheeze, and cough.

DETD . . . by day 3, reaching maximum in day 7. Such symptomatic improvement is totally unexpected particularly in patients with allergic rhinitis, **asthma** and laryngeal edema.

DETD . . . stop all other forms of therapy, including steroids. Hence the present invention is useful as a treatment and/or prevention of

allergy and asthma.

DETD [0080] Side effects: few are mentioned in the manufacturer's leaflet, glycoposphopeptical is not contraindicated for **asthma** or **allergy**, no other side effects were noticed during this short course of therapy.

DETD [0081] Stage IV: Nine patients age range 36-72 with chronic severe **asthma** of a duration ranging between 1-32 years, all of whom were on a maximal dose of broncodilators (as recommended by. . .

DETD [0094] Hypersecretion of heavy mucus or sputum, resulting in mucus-related symptoms, is characteristic of **asthma**. The eosinophil levels in the sputum are generally found to correlate with the severity of the disease. The sputum produced. . .

DETD [0115] Need for traditional forms of **asthma** therapy

DETD . . . mild, being manifested only in some shortness of breath, with mild coughing and small amounts of sputum. Traditional forms of **asthma** therapy were required only when the subjects were suffering from colds. At least eight out of the ten subjects were. . .

DETD [0119] Conclusion: Glycoposphopeptical is an agent that can be used in treating **asthma** of all types and severity, allergic/ perennial rhinitis, and other **allergies**. This short-term therapy produce Long-term effect

DETD . . . love-in-the-mist) is an equivalent to glycoposphopeptical. The use of the pure seeds of Nigella sativa for the preparation of an **asthma** and **allergy** agent in a concentration which was found to perform substantially the same function in substantially the same way to obtain. . .

CLM What is claimed is:

1. Use of glycoposphopeptical for the treatment and/or prophylaxis of **allergy/asthma** for administration to a mammal such as a human in need of such treatment.

2. Use of glycoposphopeptical for the preparation of an **asthma** /**allergy** drug 7 such as extrinsic, intrinsic or mixed **asthma**, allergic and perennial rhinitis, allergic conjunctivitis, chronic urticaria, atopic dermatitis, and/or laryngeal oedema, to be administered to a mammal such. . .

7. The use of the pure seeds of Nigella sativa for the preparation of an **asthma** and **allergy** agent in a concentration which was found to perform substantially the same function in substantially the same way to obtain. . .

14. The manufacture of a diagnostic kit to diagnose **allergy** and **asthma** and to asses the severity Of the disease, using of a quantitative serum interferon concentration measurement.

. . . for the treatment and/or prophylaxis of diseases characterized by a body immune defensive mechanism is Cell Mediated Immunity as viral **respiratory** tract infections such as, but not limited to influenza and common cold, other viral infections.

18. A method of treatment of viral **respiratory** tract infections such as, but not limited to influenza and common cold, other viral infections comprising the administration to a. . .

IT 87139-86-4, Immuferon

(glycoposphopeptical or Nigella sativa seeds for asthma/allergy therapy targeting t-lymphocytes and/or eosinophils)

L3 ANSWER 7 OF 7 TOXCENTER COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:188822 TOXCENTER

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DOCUMENT NUMBER: CA13315202992A

TITLE: Glycoposphopeptical or Nigella sativa seeds for **asthma/allergy** therapy that targets T-lymphocytes and/or eosinophils

AUTHOR(S): Nassief, Nida Abdul-Ghani

CORPORATE SOURCE: ASSIGNEE: James, David
 PATENT INFORMATION: WO 2000051580 A2 8 Sep 2000
 SOURCE: (2000) PCT Int. Appl., 28 pp.
 CODEN: PIXXD2.
 COUNTRY: AUSTRALIA
 DOCUMENT TYPE: Patent
 FILE SEGMENT: CAPLUS
 OTHER SOURCE: CAPLUS 2000:627968
 LANGUAGE: English
 ENTRY DATE: Entered STN: 20011116
 Last Updated on STN: 20020326

- AB A pharmaceutical compn. for the treatment and/or prophylaxis of diseases caused by type I hypersensitivity reactions consisting essentially of glycoposphopeptical, or pure Nigella Sativa seeds, in a concn. which stimulate Th1 lymphocytes and selectively switch-off the eosinophilic airway inflammation. A method of treatment of **allergy** using Th1 stimulating agents, to be administered to a mammal such as human in need of such treatment in a shot of 5 days only, resulted in significant decrease in symptom score started day 3, and in sputum eosinophils by day 14, followed by long-term clin. remission of a mean of 6 mo. The BCG-like Th1 stimulation is also used in treating diseases in which the body defensive mechanism is a cell-mediated immunity, including viral infections, including influenza and common cold, chronic and recurrent urinary tract infection, pelvic inflammatory diseases as neuroimmune appendicitis, cancer, Crohn's disease and facial palsy.
- TI Glycoposphopeptical or Nigella sativa seeds for **asthma/ allergy** therapy that targets T-lymphocytes and/or eosinophils
- AB. . . seeds, in a concn. which stimulate Th1 lymphocytes and selectively switch-off the eosinophilic airway inflammation. A method of treatment of **allergy** using Th1 stimulating agents, to be administered to a mammal such as human in need of such treatment in a. . .
- ST Miscellaneous Descriptors
 glycoposphopeptical immunostimulant cell mediated immunity;
allergy T cell eosinophil glycoposphopeptical immunostimulant;
asthma T cell eosinophil glycoposphopeptical immunostimulant
- RN 87139-86-4 (Immunoferon)

Record: 5

Title: [The clinical evaluation of glycoposphopeptical (Immunoferon) as combined treatment in patients with chronic lung disease]

Transliterated Title: Valoración clínica de glicofosopeptical (Immunoferon) como tratamiento asociado en pacientes afectos de enfermedad pulmonar crónica.

Author(s): Marcos Sánchez F; Rodríguez Gallego C; Celdrán Gil J; Durán Pérez-Navarro A

Source: Anales de medicina interna : organo oficial de la Sociedad Espanola de Medicina Interna [An Med Interna] 1989 Dec; 6 (12), pp. 657-8.

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MeSH Terms: Calcium Phosphates/*therapeutic use
Glycopeptides/*therapeutic use
Lung Diseases, Obstructive/*drug therapy
Aged; Drug Evaluation; Drug Therapy, Combination; Female; Human; Male; Middle Age

CAS Registry No.: 0 (Calcium Phosphates)
0 (Glycopeptides)
87139-86-4 (Immunoferon)

Revision Date: 20001218

Entry Date(s): *Date Created:* 19911016 *Date Completed:* 19911016

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acuerdo a la clasificación de Ann Arbor corresponde a un estadio IV.

Los criterios de Dawson et al. para definir los LNH de origen gastrointestinal son: 1) ausencia de adenopatías periféricas y mediastínicas; 2) normalidad en el recuento hematimétrico (no infiltración de médula ósea); 3) predominio de lesiones digestivas con afectación sólo de ganglios regionales; 4) no infiltración de hígado ni bazo (2). Según éstos sólo puede considerarse LNH de origen gastrointestinal los estadios IE y IIE de Ann Arbor. Esta definición restrictiva no se sigue actualmente por la mayoría de los autores, que prefieren los criterios de Lewin et al, según los cuales un LNH se considera de origen gastrointestinal cuando al diagnóstico hay predominio de lesiones linfomatosas en tubo digestivo y/o predominio de manifestaciones clínicas digestivas provocadas por la localización gastrointestinal del LNH (4). Esta opción, más clínica y práctica, permite incluir como LNH gastrointestinal los estadios IIIE y IV de Ann Arbor. Consideramos, por tanto, que es de acuerdo a los criterios de Lewin et al, y no a los de Dawson et al, como puede considerarse el presente LNH como de origen gástrico.

La frecuente asociación de LNH gástrico y del anillo de Waldeyer aconsejan la exploración de esta región (5).

Respecto de la revisión de la literatura, 11 casos de LNH y adenocarcinoma gástricos simultáneos o sincrónicos, remitimos a los autores un caso más (inmunocitoma y adenocarcinoma gástricos) referido por Planker et al que recogen 32 casos de la literatura (6).

Las referencias sobre la asociación sincrónica y metacrónica de adenocarcinoma gástrico y LNH son escasas. Moertel y Hagedorn revisaron 120 casos de leucemia y LNH ganglionar asociados simultáneamente a una neoplasia sólida y en sólo 3 ocasiones ésta correspondió a un adenocarcinoma gástrico (7). También es poco frecuente la aparición de un adenocarcinoma de estómago en el curso de un LNH ganglionar; McDougall et al. observaron en 630 casos de LNH con un seguimiento mediano de más de 3 años la aparición de 4 adenocarcinomas gástricos, y concluyen, como la mayoría de los autores, que la presencia de un LNH no predispone a la aparición de una segunda neoplasia (8). Por último, la aparición de un adenocarcinoma de estómago años después del diagnóstico y tratamiento de un LNH gástrico sólo se ha descrito en 17 ocasiones (9).

A pesar de que se han involucrado factores tales como la inmunodepresión tumoral y la carcinogénesis del tratamiento oncológico en la explicación de las diversas variedades de esta asociación, estamos de acuerdo con los autores en que no existen fundamentos patogénicos claros ni epidemiológicos suficientes para entender esta combinación excepcional, salvo el puro capricho de la naturaleza que asocia una neoplasia prevalente, adenocarcinoma gástrico, con un LNH.

C. GARCIA GIRON, R. DIAZ OTAZU *, M. ALDAMIZ **, J. FELIU ***

*Oncología Médica. * Anatomía Patológica. ** Medicina Interna. Hospital Txagorritxu. Vitoria. *** Oncología Médica. Hospital La Paz. Madrid.*

1. Hernández Batuecas I, Pérez Arellano JL, Sánchez Sánchez R, González Sanmartín F, Paz Bouzza JI, González Villarán L. Doble neoplasia gástrica (linfoma/adenocarcinoma) asociada a déficit de alfa-2-antitripsina. Presentación de un caso y revisión de la literatura. *An Med Intern (Madrid)* 1989; 6: 29-32.
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Valoración clínica de glicofosfopeptical (Inmunoforon[®]) como tratamiento asociado en pacientes afectos de enfermedad pulmonar crónica

Sr. Director:

El glicofosfopeptical (Inmunoforon[®]), también conocido por AM3 es un polisacárido glucomano extraído mediante procesos fermentativos de la pared celular de una cepa de *Candida utilis* y absorbido en una matriz inorgánica de fosfato y sulfato cálcico. Es farmacológicamente definido como un modificador de la respuesta biológica (BRM), con características de inmunomodulación sobre el comportamiento de macrófagos (1), polimorfonucleares y células NK.

Diversos estudios han demostrado una disminución del número de recidivas por patología infecciosa en pacientes afectos de procesos crónicos pulmonares y de la esfera O.R.L. (2,3,4,5).

En base a estos datos decidimos utilizar el fármaco en un grupo de 16 pacientes (hasta este momento), 12 hombres (75%) y 4 mujeres. Las edades estaban comprendidas entre 55 y 78 años con una edad media de 68. Todos estaban diagnosticados de enfermedad pulmonar obstructiva crónica, 4 tenían bronquiectasias bilaterales y otros 4 lesiones residuales a tuberculosis pulmonar. Todos los enfermos se caracterizaban por frecuentes agudizaciones tras procesos presuntamente infecciosos, lo que motivaba múltiples consultas y reiterados ingresos.

Se procedió a la administración de 3 cápsulas al día de glicofosfopeptical (Inmunoforon[®]) como tratamiento asociado al que previamente llevaban (broncodilatadores, etc.). Se efectuaron controles clínicos mensuales y en el caso de presentar agudizaciones. Se valoraron parámetros clínicos (incremento de tos y de disnea, expectoración purulenta, fiebre). Las crisis se valoraban como (1: leve. 2: moderada. 3: grave o severa y 4: muy severa). Asimismo se solicitó al enfermo su opinión sobre la eficacia del fármaco (nula, moderadamente buena, buena y muy buena). A los 3 meses de iniciado el tratamiento el número de crisis mensuales había disminuido a 1 (previamente 1,5), el consumo de antibióticos y corticoides había disminuido en este colectivo. 4 enfermos (25%) valoraron los resultados del fármaco como muy buenos, 2 (12,5%) de buenos, 3 (18,75%) de moderadamente buenos y 7 (43,75%) de nulos. Pese a tratarse de una serie muy pequeña y al no existir un grupo control los resultados son difícilmente valorables, pero parecen mostrar un efecto moderadamente beneficioso del glicofosfopeptical (Inmunoforon[®]) como tratamiento asociado en pacientes afectos de enfermedades crónicas pulmonares caracterizados por presentar múltiples agudizaciones por presuntos procesos infecciosos.

F. MARCOS SANCHEZ, C. RODRIGUEZ GALLEGU,
J. CELDRAN GIL, A. DURAN PEREZ-NAVARRO

Servicio de Medicina Interna del Hospital del Insalud de Talavera de la Reina (Toledo).

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5. Wischnik A. Profilaxis con un modificador de la Respuesta Biológica en las bronconeumopatías crónicas. *Farmacoterapia* 1986; 2: 257-261.

Hiponatremia e hipertensión arterial

Sr. Director:

El Dr. Hergueta García de Guadiana G. et al. ha presentado recientemente en su revista un interesante artículo referente a la utilidad del verapamil versus clortalidona en el tratamiento de pacientes afectados de hipertensión leve-moderada (1).

En el apartado de resultados nos llama la atención el nivel extraordinariamente bajo de las cifras de sodio plasmático con valores entre 116 y 123 mEq/l (tabla II de dicho estudio), sin embargo el potasio plasmático se encuentra en límites normales. Si dichas cifras de natremia no son un error de transcripción (lo más probable en nuestra opinión), contraindicaría un tratamiento con diuréticos e incluso exigiría un estudio detenido de su etiología previamente a cualquier tratamiento que pudiera modificar el volumen extracelular.

Creemos que al tratarse de un estudio que presenta gran interés tanto en el medio intrahospitalario como extrahospitalario, aclarar este aspecto puede ser interesante.

F. MARCOS SANCHEZ, C. RODRIGUEZ GALLEG0

Servicio de Medicina Interna del Hospital del Insalud de Tulavera de la Reina (Toledo).

1. Hergueta García de Guadiana G, Paumard Fraguas A. Efectos de un antagonista del calcio, verapamil, sobre la hipertensión arterial esencial leve-moderada. *An Med Intern (Madrid)* 1989; 6: 15-18.

Intoxicación por talio: Problema actual

Sr. Director:

Las sales de talio, usadas hasta su prohibición doméstica, como agente depilatorio y eficaz raticida (1) provocan tras su ingestión accidental o premeditada una severa intoxicación, que si bien compromete preferentemente el sistema nervioso, induce un fallo multiorgánico precipitando en muchos casos la muerte del enfermo (2).

Presentamos la descripción de un caso de intoxicación aguda por talio estudiado en nuestro centro, cuya relevancia, independiente del interés clínico que supone el análisis de un proceso infrecuente, estriba en la constatación de la presencia de agentes en el mercado que puedan contener dicho elemento, y que en el caso de nuestra paciente no pudo ser identificado.

La enferma de 30 años de edad, consultó en nuestro servicio por una clínica de 2 semanas de evolución consistente en: parestias dolorosas en ambas plantas con carácter ascendente hasta raíz de miembros inferiores y discreto déficit motor, dolor abdominal difuso, vómitos, estreñimiento pertinaz, trastornos del comportamiento con estado de agitación, y alopecia progresiva iniciada una semana tras el comienzo de los síntomas.

Al ingreso la enferma presentaba taquicardia sinusal a 130 lpm destacando en la exploración clínica: alopecia generalizada, ritmo cardíaco de galope, dolor a la presión en epi y mesogastrio con abdomen blando, depilación en miembros y axilas, discreta disminución de la fuerza distal en piernas, hiporreflexia aquilea y ro-

tuliana, hiperestesia en tercio distal de ambos miembros inferiores, área de hipoestesia en cara externa de muslos, e importante estado de agitación.

Los exámenes biológicos realizados fueron normales a excepción de sedimento urinario con 150 hematíes y 20 leucocitos por campo.

El E.C.G. de ingreso presentó taquicardia sinusal a 130 lpm con ondas T invertidas en las derivaciones DII, DIII, a VF y todas las precordiales. Los E.E.G. y electromiograma realizados fueron informados respectivamente como: polineuropatía de predominio sensitivo tipo desmielinizante más intensa en miembros inferiores el primero, y presencia de ondas lentas sugerentes de afectación cerebral difusa de grado medio el segundo. En base a los datos previamente referidos y ante la sospecha de intoxicación por metales pesados, se realizaron determinaciones para plomo, arsénico, y talio, resultando patológica esta última con un nivel en orina 120 $\mu\text{gr}/100\text{ cm}^3$. Una vez confirmada la intoxicación por talio se procedió a nuevo interrogatorio minucioso para conocer el producto causante de la misma, sin obtener la información deseada.

En el momento actual, 1 año tras el episodio tóxico, y medianamente sólo tratamiento sintomático, la enferma se encuentra sana y sin vestigios de enfermedad.

Históricamente las sales de talio han tenido aplicaciones industriales, santiarias, domésticas, y de uso cosmético, si bien, sólo se han descrito intoxicaciones severas en los tres últimos casos (3).

La dosis letal media es aproximadamente de 1 gr en adulto, ejerciendo su acción tóxica a través de un trastorno mitocondrial, probablemente favorecido por el comportamiento mimético con ión potasio, con el que compete en el sistema de transporte de membrana (4). Su absorción dérmica y gastrointestinal es rápida con un proceso cíclico de reabsorción-secreción en el último caso. Nosotros no pudimos constatar el producto ni la vía de administración en la enferma, aunque ésta había utilizado 15 días antes una crema de aplicación dérmica, cuya composición artesanal y finalidad de uso se nos ocultó.

El comienzo de los síntomas suele ser insidioso, alcanzando un máximo en la segunda o tercera semana, como se puede apreciar en nuestra paciente, para alcanzar posteriormente una declinación o la muerte en los casos graves.

La observación clínica descrita recoge prácticamente el conjunto sintomático de todos los órganos afectados habitualmente, con compromiso de los tegumentos, trastornos neurológicos centrales manifestados por anomalías en el comportamiento, neuropatía periférica de predominio sensitivo, trastornos en el ritmo cardíaco con signos de isquemia miocárdica, nefropatía por presunta lesión de epitelio tubular, y disfunción gastrointestinal con náuseas, vómitos, estreñimiento pertinaz y dolor abdominal.

La dosificación de talio en orina no fue conocida, por problemas técnicos, hasta el decimosegundo día de ingreso, cuando la enferma había iniciado una clara mejoría, siendo éste el motivo de no aplicar tratamiento específico (5,6,7,8). Pese a que el talio puede ser medido en sangre 12 h tras la ingestión de 1 gr, encontrando niveles próximos a los 30 $\mu\text{gr}/100\text{ cm}^3$, es procedimiento habitual realizar la determinación en orina, ya que permanece detectable hasta 3 meses tras la intoxicación, siendo útil para diagnósticos retrospectivos precoces como en el caso de nuestra paciente (2).

El tratamiento, iniciado con lavado gástrico de soluciones que contengan yoduro sódico para hacer no absorbible la sal de talio, está fundamentado en el empleo de Berliner-Blue (ferrihexacianato) como neutralizante del ciclo intestinal, hemodiálisis, diuresis forzada y hemoperfusión (5,6,7). Como conclusión consideramos que, pese a su infrecuencia, todo enfermo portador de una neuropatía periférica de predominio sensitivo de causa desconocida, debe ser sometido a estudios que incluyan determinación de talio en sangre y orina, con el fin de iniciar tratamiento precoz que evite la muerte del paciente.

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